

Appl. No. 10/058,069  
Amendment dated February 10, 2005  
Reply to Non-Final Official Action of August 10, 2004  
Attorney Ref. No.: 037003-0280727

## II. REMARKS

### Preliminary Remarks:

#### Amendment of the specification

The reference in the first paragraph to priority applications, and references in the description to unpublished applications, are amended as requested in the official action.

#### Amendment of the claims

Claims 20, 29, and 38 are amended, claims 1-19, 21-28, 30-37, and 41-50 are canceled, and new claims 51-79 are added.

Claim 1 is amended to specify that the disorder to be treated is a neoplastic disorder, and claims 1 and 29 are amended to specify that the dimeric antibody binds specifically to TAG-72, and comprises two antibodies that are non-covalently associated to form a tetravalent antibody dimer, wherein each of the antibodies in the dimer comprises two antibody heavy chain polypeptides and two antibody light chain polypeptides, and has two antigen-binding sites; wherein one or more of the antigen binding sites of the tetravalent antibody dimer binds specifically to TAG-72; and wherein the C<sub>H</sub>2 domain is deleted from each of the four antibody heavy chain polypeptides in the dimeric antibody.

New claims 51-63 specify features and embodiments of the kit of claim 20 disclosed in the specification, and new claims 64-75 similarly specify features and embodiments of the dimeric antibody of claim 29. New claims 76-79 specify disclosed cytotoxic agents according to claim 38.

### Patentability Remarks:

#### 35 U.S.C. §112, Second Paragraph

References to "modified" antibodies, a "monomeric subunit," "homodimer," "heterodimer," and "associated" in the claims that were the basis for rejection under 35 U.S.C. §112, Second Paragraph, have been removed by the amendment.

#### 35 U.S.C. §112, First Paragraph

Claims 20-24, 26-32, 34, and 38-40 were rejected under 35 U.S.C. §112, First Paragraph, because the specification is allegedly enabling only for a dimeric antibody comprising two polypeptide chains having heavy and light chain variable domains and 6 CDRs.

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The claims are amended to specify that the dimeric antibody of the claimed invention comprises two antibodies that are associated to form a tetravalent antibody dimer, and that each of the antibodies in the dimer comprises two antibody heavy chain polypeptides and two antibody light chain polypeptides and has two antigen-binding sites; that one or more of the antigen binding sites of the tetravalent antibody dimer binds specifically to TAG-72; and that the C<sub>H</sub>2 domain is deleted from each of the four antibody heavy chain polypeptides in the dimeric antibody. The claims clearly specify that the antibody binds specifically to TAG-72, from which a person of ordinary skill in the art would recognize that the antibody comprises functional CDRs. The applicants respectfully submit that the presence of functional CDRs in the antibody need not be expressly described in the claims. Withdrawal of the rejection in view of the amendment of claims 20 and 29 as discussed above is respectfully requested.

35 U.S.C. §§102(a) and 102(b)

Claims 29-34 and 36-40 were rejected under 35 U.S.C. §102(a) as being anticipated by Goel et al. (a), and by Goel et al. (b).

Claims 29-34 and 36-40 were rejected under 35 U.S.C. §102(b) as being anticipated by Pavlinkova (a), and by Pavlinkova (b).

Claims 29-34 and 36-37 were rejected under 35 U.S.C. §102(b) as being anticipated by Mezes et al. (WO 94/13806, 1994).

Claims 29-33 and 36-40 were rejected under 35 U.S.C. §102(b) as being anticipated by Slavin-Chiorini et al. (1993).

35 U.S.C. §103(a)

Claims 20-34 and 36-40 were rejected under 35 U.S.C. §103(a) as being obvious in view of Goel et al. (a); in view of Goel et al. (b); in view of Pavlinkova (a); in view of Pavlinkova (b); or in view of Mezes et al. (WO 94/13806, 1994) taken with Anderson et al. (U.S. Patent No. 6,348,581).

Claims 20-26, 28-33, and 36-40 were rejected under 35 U.S.C. §103(a) as being obvious in view of Slavin-Chiorini et al. (1993).

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As amended herein, none of the cited references described or suggested the claimed invention, wherein two antibodies are non-covalently associated to form a tetravalent antibody dimer that comprises four heavy chain polypeptides and four light chain polypeptides. The specification of the present application clearly defines a dimeric antibody according to the claimed invention as being a tetravalent complex that comprises four antigen-binding sites. For example, see the description in the paragraph beginning at line 4 on page 7:

"The present invention is predicated, at least in part, on the fact that antibodies which are immunoreactive with antigens associated with physiological disorders or abnormalities may be modified or altered to provide dimeric constructs having enhanced biochemical characteristics and improved efficacy when used in therapeutic protocols. In this regard it has surprisingly been found that standard antibodies, modified according to the present invention, form monomeric subunits which spontaneously assemble or associate non-covalently to form stable dimeric constructs. If the associated monomeric subunits are the same the resulting dimeric construct will have four identical binding sites and is termed a homodimer for the purposes of this application. Conversely, if the associated monomeric subunits are different (e.g. derived from separate antibodies) than the resulting dimeric construct will have two binding sites for one antigen and two binding sites for a second antigen and, for the purposes of this application will be termed a heterodimer. In any event, the dimeric or tetravalent construct or antibody (four heavy chains and four light chains, H<sub>4</sub>L<sub>4</sub>) may be used as described in the instant application to treat a variety of disorders."

See also, the description on in the paragraph beginning at line 21 on page 20:

"the dimeric assemblies disclosed herein may be likened to two associated Y's (H<sub>4</sub>L<sub>4</sub>) so there will be four binding sites. Hence the term "tetravalent" antibodies."

Each of the antibodies described in the cited prior art references has no more than two sets of light and heavy chains, and so belongs to the class of "monomeric" antibodies described in the present application (e.g., see page 25, line 13). Given that none of the prior art references described or suggested a tetravalent antibody dimer as described in the amended claims, which comprises two non-covalently associated antibodies, and has a total of four heavy chain and four light chain polypeptides, the applicants submit that the claimed invention is neither anticipated by, or obvious in view of the cited references. Withdrawal of the rejections of the claims under 35 U.S.C. §§102(a), 102(b), and 103(a) stated in the official action is therefore respectfully requested.

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**Conclusion**

All rejections having been addressed, it is respectfully submitted that the present application is in condition for allowance and a Notice to that effect is earnestly solicited. If any points remain in issue, which the examiner feels may be best resolved through a personal or telephone interview, he is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,  
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